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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
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ART UNIT	PAPER NUMBER
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/529,221	ROBERT ET AL.	
	Examiner	Art Unit	
	MARIANNE DIBRINO	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11/30/09 & 4/9/10*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,13,17,28,36-41,46 and 49-65* is/are pending in the application.

4a) Of the above claim(s) *5-7,9,13,17,28,36-39,41,46,53,56,58 and 60-65* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,8,10,11,40,49-52,54,55,57 and 59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendments and responses filed 11/30/09 and 4/9/10 are acknowledged and have been entered.

2. Applicant is reminded Applicant's election with traverse of Group I and without traverse of the species of CD1d complex comprising the antigen α–GalCer fused to an scFv antibody fragment with specificity for Her2/neu, and wherein the said complex does not further comprise a costimulatory molecule, in Applicant's amendment and response filed 2/23/09 and Applicant's response filed 6/2/09.

Applicant's election without traverse of the following species: CD1d complex wherein the scFv molecule is fused to the CD1d molecule through a peptide bridge linker with an amino acid sequence of from 3 to about 30 amino acid residues, wherein said linker is SEQ ID NO: 2, and wherein the CD1d molecule is located N-terminal to the scFv molecule in Applicant's response filed 4/9/10 is acknowledged.

Claims 1-4, 8, 10, 11, 40, 49-52, 54, 55, 57 and 59 are currently being examined.

3. Applicant's amendment filed 11/30/09 has overcome the prior rejection of record of claims 1-4, 8, 10, 11 and 40 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

4. For the purpose of prior art rejections, the filing date of the instant claims 3, 4, 10, 11, 49-52, 55, 57 and 59 is deemed to be the filing date of PCT/US03/30238, *i.e.,* 9/26/03, as the foreign priority application EPO 02405838.0 does not support the claimed limitations of the instant application. The said parent application does not provide support for an antibody with specificity for the other cell surface markers EGFR type I or type II, CD19, CD22, Muc-1, PSMA or STEAP recited in instant claim 11, nor for the hydrophobic peptide recited in instant claim 3. The said parent application does not support the extracellular portion of CD1d (claim 50), or SEQ ID NO: 40 (claim 51) or 2 (claim 59), or wherein the Vl and VH domain of scFv are linked by a peptide bridge (claim 52)or the configuration recited in claim 55, or the short linker recited in claim 57.

Applicant's arguments have been fully considered, but are not persuasive.

Applicant's arguments are of record on pages 11-12 of the response filed 11/30/09.

Applicant argues that Applicant's foreign priority document 02405838.0 generally discloses the use of monoclonal antibodies specific for TAAs, and that one of ordinary skill in the art would appreciate that EGFR type I and type II, CD19, CD22, Muc-1, PSMA and STEAP are all TAAs.

However, the disclosure of a genus in a parent application is not support for a later recited species falling within that genus in a child application.

In addition, with regard to Applicant's assertion that the said foreign priority document does teach compounds comprising greater than one CD1d complex at page 4 at lines 13-14, the argument is not found persuasive.

The cited disclosure is that a general strategy will be to couple monomorphic MHC class I-related proteins to anti-TAA mAbs or fragments of mAbs in order to target them on tumor cells. At a minimum, in contrast, the prior version of instant claim 1 recited an open-ended genus of number of CD1d complexes in the claimed compound.

The Examiner acknowledges Applicant's amendment of base claim 1 to recite the CD1d complex in the singular.

5. Applicant's amendment and response filed 11/30/09 has overcome the prior rejection of record of claims 1, 2 and 40 under 35 U.S.C. 103(a) as being obvious over Donda *et al* (Cancer Immunity 8/03, 3: 11) in view of US 2002/0071842 A1 (of record) and Fujii *et al* (Nature Immunology, 9/02, 3(9): 867-875), *i.e.,* due to Applicant's amendment of base claim 1 to recite the CD1d complex in the singular.

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 3, 4, 10, 11, 49-51, 54, 55, 57 and 59 are rejected under 35 U.S.C. 103(a) as being obvious over Donda *et al* (Cancer Immunity 8/03, 3: 11, of record) in view of US 2002/0071842 A1 (of record), Fujii *et al* (Nature Immunology, 9/02, 3(9): 867-875, of record), WO 99/64597 A1 (IDS reference) and an admission in the specification at the sequence listing for SEQ ID NO: 40.

Claims 3, 4, 10 and 11 were rejected previously on the basis set forth below. Claims 49-51, 54, 55 and 57 have been newly added by Applicant's amendment filed 11/30/09.

Donda *et al* teach *in vivo* targeting of an anti-tumor antibody coupled to an antigenic MHC class I complex to induce specific growth inhibition and regression of established syngeneic tumor grafts. Donda *et al* teach that their strategy combined the advantage of the well-documented tumor targeting properties of anti-tumor antigen (*i.e.,* anti-TAA) mAbs with the known efficient and specific cytotoxic activity of CD8 T lymphocytes directed against highly antigenic MHC/peptide complexes, *i.e.,* using a Fab' fragment from a high affinity anti-TAA mAb coupled to a MHC class I containing a selected

antigenic peptide in order to target the active MHC/peptide complex on tumor cells and induce their lysis by specific CTLs. Donda *et al* further teach using an anti-ErbB-2 antibody coupled to an MHC/peptide complex (*e.g.,* ErbB-2 is also known as Her2/neu) (see entire reference).

Donda *et al* do not teach wherein the compound used for targeting and tumor cell destruction comprises a CD1d complex rather than an MHC complex, nor wherein the antigen bound to the CD1d molecule is α-GalCer, nor the linker that is SEQ ID NO: 2.

US 2002/0071842 A1 discloses a CD1d-IgG Fc fusion protein comprising a tumor antigen, or alternately comprising α-GalCer as the antigen, that binds to CD1d, and administration of a composition comprising such in order to enhance or induce protective immunity to a condition associated with the presence of the tumor antigen (*i.e.,* a cancer). US 2002/0071842 A1 discloses that CD1 molecules are evolutionarily conserved β2m-associated proteins, with a similar domain organization to class I MHC antigen presenting molecules, although CD1 molecules have a deeper and more hydrophobic antigen binding groove that do class I MHC molecules. US 2002/0071842 A1 discloses that correspondingly, while class I MHC molecules present peptide antigens, CD1 molecules can present lipids, phospholipids and glycolipids, and both human and murine CD1d molecules have been shown to present α-GalCer, a synthetic acylphytosphingolipid originally isolated from a marine sponge, and that this latter antigen is recognized by CD1d-restricted NKT cells. US 2002/0071842 A1 discloses that the CD1d may be the extracellular portion, and that a GSG linker may be present between CD1d and the antibody or antibody fragment (especially Abstract, [0011], [0012], [0030], [0031], [032]-[0035], [0039], [0046], [0055], [0080]-[0083], [0095], [0101], [0120], [0124], [0127]-[0129], [0138], [0153], [0156], [0158] and claims).

Fujii *et al* teach that NKT lymphocytes are implicated in control of resistance to tumors and that a subset of NKT cells that have an invariant TCR are restricted to CD1d. Fujii *et al* further teach that α-GalCer binds to and is presented by CD1d to NKT cells, thus having anti-tumor activity. Fujii *et al* teach that it is preferable to administer α-GalCer – pulsed dendritic cells (that express CD1d) *versus* administering free α-GalCer because the response was stronger, more prolonged and was associated with increased protection against the development of metastases with melanoma (especially abstract, introduction and discussion sections).

WO 99/64597 A1 teaches use of a $(G_4S)_3$ linker or a modified linker with the sequence GGGGSGGGGSGGGAS (SEQ ID NO: 2 recited in instant claim 59) that is used to link or fuse HLA-B7 heavy chain with β2m light chain in order to make functional MHC class I complexes (see entire reference, especially Figure 3 and abstract).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have constructed an antibody or antigen-binding antibody fragment-targeted-complex with specificity for the cell surface marker Her2/neu (ErbB-2)

similar to that taught by Donda *et al*, but rather making a CD1d/β2m/α-GalCer complex by engineering a fusion protein of CD1d with the antibody or antigen-binding fragment thereof with specificity for a cell surface marker such as the tumor antigen Her2/neu (ErbB-2) and loading α-GalCer into the antigen binding site of CD1d/β2m. It would have been prima facie obvious to have used any suitable linker such as the one taught by WO 99/64597 A1.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to produce a compound that could target tumor cells expressing Her2/neu with the said compound in order to protect against targeted tumors by activation of NKT cells, particularly in light of the teaching of Fujii *et al* that α-GalCer binds to and is presented by CD1d to NKT cells that are useful in controlling resistance to tumors, and in light of the disclosure of US 2002/0071842 A1 that an CD1d-IgG fusion protein comprising α-GalCer is useful to enhance or induce protective immunity to cancer.

The admission in the specification at the sequence listing for SEQ ID NO: 40 is that amino acid residues 1-297 are the extracellular domain of CD1d and the remaining amino acid residues 298-303 are a 6XHis tag.

While the art references do not explicitly disclose amino acid residues 1-297 of SEQ ID NO: 40 that is the limitation recited in instant claim 51, the US 2002/0071842 A1 reference does disclose using the extracellular portion of CD1d.

Therefore the claimed compound appears to be similar to the compound of the prior art absent a showing of unobvious differences. Since the Patent Office does not have the facilities for examining and comparing the composition of the instant invention to those of the prior art, the burden is on Applicant to show an unobvious distinction between the antibody of the instant invention and that of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Applicant's arguments have been fully considered but are not persuasive.

Applicant's said arguments are of record in the amendment filed 11/30/09 on pages 13-15 at section B(I).

However, Donda *et al* is appropriately cited prior art, for the reasons enunciated at item # 4 supra. Applicant is arguing the remaining references separately.

8. Applicant's amendment filed 11/30/09 has overcome the prior rejection of record of claim 8 under 35 U.S.C. 103(a) as being obvious over Donda *et al* (Cancer Immunity 8/03, 3: 11) in view of US 2002/0071842 A1 (of record) and Fujii *et al* (Nature Immunology, 9/02, 3(9): 867-875) as applied to claims 1-4, 10, 11 and 40 above, and

further in view of Pavlinkova *et al* (Cancer immunology and immunotherapy, 2000, 49(4-5): 267-275, of record).

9. Claims 1-4, 8, 10, 11, 40, 49-52, 54, 55, 57 and 59 are rejected under 35 U.S.C. 103(a) as being obvious over US 20030166277 A1 in view of US 2002/0071842 A1 (of record), Fujii *et al* (Nature Immunology, 9/02, 3(9): 867-875, of record), WO 99/64597 A1 (IDS reference) and an admission in the specification at the sequence listing for SEQ ID NO: 40.

US 20030166277 A1 discloses one or more MHC/peptide complexes linked or fused to an antibody, including a scFv wherein the Vh and Vl are linked by a peptide bridge or by disulfide bonds, that is specific for a cell surface marker, including Her2/neu, the complexes useful for treating cancer, infectious diseases, autoimmune diseases and/or allergies. US 20030166277 A1 discloses that the attachment of the MHC chains to the antibody chains may be direct or through a linker amino acid sequence of at least 3 and not more than 30 amino acid residues (see entire reference, especially abstract, [0076], [0220], Figures 1-3, [0031], [0049], [0107], [0227], [0232]).

US 20030166277 A1 does not disclose wherein the compound used for targeting and tumor cell destruction comprises a CD1d complex rather than an MHC complex, nor wherein the antigen bound to the CD1d molecule is α-GalCer.

US 2002/0071842 A1 discloses a CD1d-IgG Fc fusion protein comprising a tumor antigen, or alternately comprising α-GalCer as the antigen, that binds to CD1d, and administration of a composition comprising such in order to enhance or induce protective immunity to a condition associated with the presence of the tumor antigen (*i.e.,* a cancer). US 2002/0071842 A1 discloses that CD1 molecules are evolutionarily conserved β2m-associated proteins, with a similar domain organization to class I MHC antigen presenting molecules, although CD1 molecules have a deeper and more hydrophobic antigen binding groove that do class I MHC molecules. US 2002/0071842 A1 discloses that correspondingly, while class I MHC molecules present peptide antigens, CD1 molecules can present lipids, phospholipids and glycolipids, and both human and murine CD1d molecules have been shown to present α-GalCer, a synthetic acylphytosphingolipid originally isolated from a marine sponge, and that this latter antigen is recognized by CD1d-restricted NKT cells. US 2002/0071842 A1 discloses that the CD1d may be the extracellular portion, and that a GSG linker may be present between CD1d and the antibody or antibody fragment (especially Abstract, [0011], [0012], [0030], [0031], [032]-[0035], [0039], [0046], [0055], [0080]-[0083], [0095], [0101], [0120], [0124], [0127]-[0129], [0138], [0153], [0156], [0158] and claims).

Fujii *et al* teach that NKT lymphocytes are implicated in control of resistance to tumors and that a subset of NKT cells that have an invariant TCR are restricted to CD1d. Fujii *et al* further teach that α-GalCer binds to and is presented by CD1d to NKT cells, thus having anti-tumor activity. Fujii *et al* teach that it is preferable to administer α-GalCer –

pulsed dendritic cells (that express CD1d) *versus* administering free α-GalCer because the response was stronger, more prolonged and was associated with increased protection against the development of metastases with melanoma (especially abstract, introduction and discussion sections).

WO 99/64597 A1 teaches use of a $(G_4S)_3$ linker or a modified linker with the sequence GGGGSGGGGSGGGAS (SEQ ID NO: 2 recited in instant claim 59) that is used to link or fuse HLA-B7 heavy chain with β2m light chain in order to make functional MHC class I complexes (see entire reference, especially Figure 3 and abstract).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have constructed an antibody or antigen-binding antibody fragment-targeted-complex with specificity for the cell surface marker Her2/neu (ErbB-2) similar to that disclosed by US 20030166277 A1, but rather making a CD1d/β2m/α-GalCer complex by engineering a fusion protein of CD1d with the antibody or antigen-binding fragment thereof with specificity for a cell surface marker such as the tumor antigen Her2/neu (ErbB-2) and loading α-GalCer into the antigen binding site of CD1d/β2m. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used any suitable linker such as the ones taught by WO 99/64597 A1.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to produce a compound that could target tumor cells expressing Her2/neu with the said compound in order to protect against targeted tumors by activation of NKT cells, particularly in light of the teaching of Fujii *et al* that α-GalCer binds to and is presented by CD1d to NKT cells that are useful in controlling resistance to tumors, and in light of the disclosure of US 2002/0071842 A1 that an CD1d-IgG fusion protein comprising α-GalCer is useful to enhance or induce protective immunity to cancer.

The admission in the specification at the sequence listing for SEQ ID NO: 40 is that amino acid residues 1-297 are the extracellular domain of CD1d and the remaining amino acid residues 298-303 is a 6XHis tag.

While the art references do not explicitly disclose amino acid residues 1-297 of SEQ ID NO: 40 that is the limitation recited in instant claim 51, the US 2002/0071842 A1 reference does disclose using the extracellular portion of CD1d.

Therefore the claimed compound appears to be similar to the compound of the prior art absent a showing of unobvious differences. Since the Patent Office does not have the facilities for examining and comparing the composition of the instant invention to those of the prior art, the burden is on Applicant to show an unobvious distinction between the antibody of the instant invention and that of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claims 3, 4, 8, 10, 11, 40, 49, 50, 51, 54, 55, 57 and 59 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 78 of copending Application No. 12/034,737 in view of Pavlinkova *et al* (Cancer immunology and immunotherapy, 2000, 49(4-5): 267-275), US 2002/0071842 A1 (of record), Donda *et al* (Cancer Immunity 8/03, 3: 11) and WO 99/64597 A1 (IDS reference) as evidenced by an admission in the specification at the sequence listing for SEQ ID NO: 40.

This rejection is necessitated by Applicant's amendment filed 11/30/09 that amends base claim 1 and adds new claims 49-52, 54, 55, 57 and 59.

Claim 78 of copending Application No. 12/034,737 is drawn to a CD1d complex comprising a soluble CD1d polypeptide/β2m and a ceramide-like glycolipid antigen bound to the CD1d/β2m and a carrier.

The said claim does not recite an antibody or scFv fragment thereof portion specific for a cell surface marker such as Her2/neu fused to the CD1d complex.

Pavlinkova *et al* teach that the major advantages of scFv molecules are their excellent penetration into tumor tissue, rapid clearance rate and much lower exposure to normal organs than occurs with intact antibody (especially abstract).

US 2002/0071842 A1 discloses a CD1d-IgG Fc fusion protein comprising a tumor antigen, or alternately comprising α-GalCer as the antigen, that binds to CD1d, and administration of a composition comprising such in order to enhance or induce protective immunity to a condition associated with the presence of the tumor antigen (*i.e.,* a cancer). US 2002/0071842 A1 discloses that CD1 molecules are evolutionarily conserved β2m-associated proteins, with a similar domain organization to class I MHC antigen presenting molecules, although CD1 molecules have a deeper and more hydrophobic antigen binding groove that do class I MHC molecules. US 2002/0071842 A1 discloses that correspondingly, while class I MHC molecules present peptide antigens, CD1 molecules can present lipids, phospholipids and glycolipids, and both human and murine CD1d molecules have been shown to present α-GalCer, a synthetic acylphytosphingolipid originally isolated from a marine sponge, and that this latter antigen is recognized by CD1d-restricted NKT cells. US 2002/0071842 A1 discloses that the CD1d may be the extracellular portion, and that a GSG linker may be present between CD1d and the antibody or antibody fragment (especially Abstract, [0011], [0012], [0030], [0031], [032]-[0035], [0039], [0046], [0055], [0080]-[0083], [0095], [0101], [0120], [0124], [0127]-[0129], [0138], [0153], [0156], [0158] and claims).

Donda *et al* teach *in vivo* targeting of an anti-tumor antibody coupled to an antigenic MHC class I complex to induce specific growth inhibition and regression of established syngeneic tumor grafts. Donda *et al* teach that their strategy combined the advantage of the well-documented tumor targeting properties of anti-tumor antigen (*i.e.,* anti-TAA) mAbs with the known efficient and specific cytotoxic activity of CD8 T lymphocytes directed against highly antigenic MHC/peptide complexes, *i.e.,* using a Fab' fragment from a high affinity anti-TAA mAb coupled to a MHC class I containing a selected antigenic peptide in order to target the active MHC/peptide complex on tumor cells and induce their lysis by specific CTLs. Donda *et al* further teach using an anti-ErbB-2 antibody coupled to an MHC/peptide complex (*e.g.,* ErbB-2 is also known as Her2/neu) (see entire reference).

WO 99/64597 A1 teaches use of a $(G_4S)_3$ linker or a modified linker with the sequence GGGGSGGGGSGGGAS (SEQ ID NO: 2 recited in instant claim 59) that is used to link or fuse HLA-B7 heavy chain with β2m light chain in order to make functional MHC class I complexes (see entire reference, especially Figure 3 and abstract).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have added an scFv anti-Her2/neu targeting antibody fragment such as the scFv fragment taught by Pavlinkova *et al* with specificity for Her2/neu such as taught by Donda *et al* to the CD1d complex of claim 78 of copending Application No. 12/034,737 and to have used α-GalCer taught by Donda *et al* and disclosed by US

2002/0071842 A1 as the ceramide-like glycolipid antigen. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used a linker such as the one disclosed by US 2002/0071842 A1 and to have used the extracellular portion of CD1d as disclosed by US 2002/0071842 A1. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used any suitable linker such as the one taught by WO 99/64597 A1.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to produce an improved reagent for control of tumors, *i.e.,* a CD1d complex that could be targeted to tumor cells bearing the Her2/neu tumor associated antigen.

The admission in the specification at the sequence listing for SEQ ID NO: 40 is that amino acid residues 1-297 are the extracellular domain of CD1d and the remaining amino acid residues 298-303 is a 6XHis tag.

While the art references do not explicitly disclose amino acid residues 1-297 of SEQ ID NO: 40 that is the limitation recited in instant claim 51, the US 2002/0071842 A1 reference does disclose using the extracellular portion of CD1d.

Therefore the claimed compound appears to be similar to the compound of the prior art absent a showing of unobvious differences. Since the Patent Office does not have the facilities for examining and comparing the composition of the instant invention to those of the prior art, the burden is on Applicant to show an unobvious distinction between the antibody of the instant invention and that of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

This is a provisional obviousness-type double patenting rejection.

Applicant's arguments have been fully considered but are not persuasive.

Applicant's arguments are of record in the amendment filed 11/30/09 on pages 16-17 at section C.

However, the double patenting rejection is not the last remaining rejection.

12. Claims 1-4, 8, 10, 11, 40, 49, 50, 51, 54, 55, 57 and 59 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 78 of copending Application No. 12/034,737 in view of Pavlinkova *et al* (Cancer immunology and immunotherapy, 2000, 49(4-5): 267-275), US 2002/0071842 A1 (of record), US 20030166277 A1, and WO 99/64597 A1 (IDS reference), as evidenced by an admission in the specification at the sequence listing for SEQ ID NO: 40.

This rejection is necessitated by Applicant's amendment filed 11/30/09 that amends base claim 1 and adds new claims 49-52, 54, 55, 57 and 59.

Claim 78 of copending Application No. 12/034,737 is drawn to a CD1d complex comprising a soluble CD1d polypeptide/β2m and a ceramide-like glycolipid antigen bound to the CD1d/β2m and a carrier.

The said claim does not recite an antibody or scFv fragment thereof portion specific for a cell surface marker such as Her2/neu fused to the CD1d complex.

Pavlinkova *et al* teach that the major advantages of scFv molecules are their excellent penetration into tumor tissue, rapid clearance rate and much lower exposure to normal organs than occurs with intact antibody (especially abstract).

US 2002/0071842 A1 discloses a CD1d-IgG Fc fusion protein comprising a tumor antigen, or alternately comprising α-GalCer as the antigen, that binds to CD1d, and administration of a composition comprising such in order to enhance or induce protective immunity to a condition associated with the presence of the tumor antigen (*i.e.,* a cancer). US 2002/0071842 A1 discloses that CD1 molecules are evolutionarily conserved β2m-associated proteins, with a similar domain organization to class I MHC antigen presenting molecules, although CD1 molecules have a deeper and more hydrophobic antigen binding groove that do class I MHC molecules. US 2002/0071842 A1 discloses that correspondingly, while class I MHC molecules present peptide antigens, CD1 molecules can present lipids, phospholipids and glycolipids, and both human and murine CD1d molecules have been shown to present α-GalCer, a synthetic acylphytosphingolipid originally isolated from a marine sponge, and that this latter antigen is recognized by CD1d-restricted NKT cells. US 2002/0071842 A1 discloses that the CD1d may be the extracellular portion, and that a GSG linker may be present between CD1d and the antibody or antibody fragment (especially Abstract, [0011], [0012], [0030], [0031], [032]-[0035], [0039], [0046], [0055], [0080]-[0083], [0095], [0101], [0120], [0124], [0127]-[0129], [0138], [0153], [0156], [0158] and claims).

US 20030166277 A1 discloses one or more MHC/peptide complexes linked or fused to an antibody, including a scFv wherein the Vh and Vl are linked by a peptide bridge or by disulfide bonds, that is specific for a cell surface marker, including Her2/neu, the complexes useful for treating cancer, infectious diseases, autoimmune diseases and/or allergies. US 20030166277 A1 discloses that the attachment of the MHC chains to the antibody chains may be direct or through a linker amino acid sequence of at least 3 and not more than 30 amino acid residues (see entire reference, especially abstract, [0076], [0220], Figures 1-3, [0031], [0049], [0107], [0227], [0232]).

WO 99/64597 A1 teaches use of a $(G_4S)_3$ linker or a modified linker with the sequence GGGGSGGGGSGGGAS (SEQ ID NO: 2 recited in instant claim 59) that is used to link or fuse HLA-B7 heavy chain with β2m light chain in order to make functional MHC class I complexes (see entire reference, especially Figure 3 and abstract).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have added an scFv anti-Her2/neu targeting antibody fragment such as the scFv fragment taught by Pavlinkova *et al* or US 20030166277 A1 with specificity for Her2/neu as disclosed by US 20030166277 A1 to the CD1d complex of claim 78 of copending Application No. 12/034,737 and to have used α-GalCer disclosed by US 2002/0071842 A1 as the ceramide-like glycolipid antigen. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used a linker such as the one disclosed by US 2002/0071842 A1 or by US 20030166277 A1 and to have used the extracellular portion of CD1d as disclosed by US 2002/0071842 A1. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used any suitable linker such as the one taught by WO 99/64597 A1.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to produce an improved reagent for control of tumors, *i.e.,* a CD1d complex that could be targeted to tumor cells bearing the Her2/neu tumor associated antigen.

The admission in the specification at the sequence listing for SEQ ID NO: 40 is that amino acid residues 1-297 are the extracellular domain of CD1d and the remaining amino acid residues 298-303 is a 6XHis tag.

While the art references do not explicitly disclose amino acid residues 1-297 of SEQ ID NO: 40 that is the limitation recited in instant claim 51, the US 2002/0071842 A1 reference does disclose using the extracellular portion of CD1d.

Therefore the claimed compound appears to be similar to the compound of the prior art absent a showing of unobvious differences. Since the Patent Office does not have the facilities for examining and comparing the composition of the instant invention to those of the prior art, the burden is on Applicant to show an unobvious distinction between the antibody of the instant invention and that of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

This is a provisional obviousness-type double patenting rejection.

13. The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned 12/034,737, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

Applicant's arguments have been fully considered but are not persuasive.

Applicant's arguments are of record in the amendment filed 11/30/09 on pages 16-17 at section C.

However, the double patenting rejection is not the last remaining rejection.

14. No claim is allowed.

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday, Tuesday, Thursday and Friday.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ram Shukla, can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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